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Investigation of Sleep-Dependent Activation-Interaction Association Network

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***Abstract*—The cortical activation and the interaction between cortical regions were considered to exist a strong correlation in recent neuroscience researches. However, such association during sleep was still unclear. The aim of the present work was to further investigate this association according to an activation-interaction association network. This study included 24 healthy individuals and all of them underwent overnight polysomnography. The absolute spectral powers of three frequency bands and the phase transfer entropy were extracted from six electroencephalogram channels. For each frequency band and sleep stage, activation-interaction association networks were built and correlation analysis was conducted by using Pearson correlation test. Results revealed the evident association between features derived from the two approaches during sleep, and as the sleep deepened, these correlation values attenuated in the alpha band, whereas the inversion happened in the delta band. This study exposed more detailed information of cortical activity during sleep, which will facilitate us to conduct research from a more comprehensive perspective, helping us make a more appropriate evaluation and explanation.**

***Clinical Relevance*—This facilitates understanding of sleep regulation mechanism and may provide a new insight for the research on sleep related diseases.**

I. Introduction

Sleep is a behavioral state which relates to the regulation of brain function and involves the adjustment of cerebral cortex activity to maintain the homeostasis of the brain network [1]. A host of researches in neuroscience and electrophysiology have explored brain activity during sleep [2]-[4]. It is a matter of common observation that electroencephalography (EEG) is widely used for cortical activity monitoring in polysomnography (PSG) in virtue of its advantages of high time resolution, long-term recording, and relatively low physiological load. Prevalent applications utilized to characterize EEG comprise network analysis performed on functional connectivity (FC) or effective connectivity (EC) and power spectral analysis patterns [5]. However, results derived from these two research approaches are analyzed separately under most conditions, while recent studies reported that strong association was found between these results [6]-[8]. Thus, with the absence of relevant research, the investigation of exploring this overlooked association during slumber may provide a comprehensive interpretation of the underlying brain mechanisms during sleep.

Power spectral density can be applied to measure the activation of the cerebral cortex and is an important metric for clinical diagnosis and research of abnormal brain diseases [9]. A number of studies have been focused on the changes of power spectral density in different sleep stages [10], and correlation between sleep- or brain-related diseases and variation in cortical power spectrum, such as the analysis of discrepancies arise in the cortical power spectrum of patients with obstructive sleep apnea during sleep [11]. Additionally, as methods commonly used for connectivity analysis, FC utilizes signals recorded in different brain regions to calculate an index that reflects the strength of the relationship between different brain regions. And EC refers to a kind of causal influence, which is directional [12]. Informatics methods were widely applied to EC analysis for further directional brain network investigation. Transfer entropy (TE), a well-known EC measure based on information theory to deal with the causal interaction between brain regions, is commonly used to study the transmission of brain information flows to reveal more brain function information [13]. From the improvement of TE, phase transfer entropy (PTE) was proposed by Lobier et al [14] and was used in this research.

In order to further investigate the association between cortical activation and network connectivity during sleep, we built an activation-interaction association network to quantify the coupling. The absolute spectral powers and the PTE were extracted from six EEG channels (Frontal lobe: F3, F4; Central: C3, C4; Occipital lobes: O1, O2) in different frequency bands and different sleep stages. Correlation analysis was done among these feature series using Pearson correlation coefficient, and an activation-interaction association network was built for each of frequency bands and sleep stages.

II. Materials and Methods

A. Participants and Data Acquisition

We enrolled 24 healthy normal subjects in our study (11 males,13 females, 18-24 years with a mean age of 19.79 ± 1.35 years). Participants were recruited from Sun Yat-sen University and had no history of nerve damage, no family history of psychiatric disorders, and no history of drug or alcohol abuse. This study was approved by the Ethics

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Committee of Guangdong 999 Brain Hospital. All procedures performed in this study were in accordance with the 1964 Helsinki declaration and its later amendments. All participants voluntarily signed an informed consent form before the experiment and were appropriately remunerated after the experiment.

B. Polysomnography

All participants underwent overnight PSG. PSG records included 6 EEG channels (F4/M1, F3/M2, C4/M1, C3/M2, O2/M1, O1/M2) placed based on the standard 10-20 system, electrooculography (EOG), electrocardiography (ECG), electromyography (EMG), oral and nasal respiratory airflow, chest and abdomen breathing movement, blood oxygen saturation. The sampling frequencies of the EEG, EOG, and EMG signals were 500 Hz, and the sampling frequencies of respiration signal and oxygen saturation were 100 Hz and 10 Hz, respectively. Sleep stages were scored by two experienced sleep technicians according to the American Academy of Sleep Medicine Scoring Manual (AASM), including non-rapid eye movement sleep (N1, N2 and N3), rapid eye movement sleep (R) and wake (W).

C. EEG Preprocessing

The EEG signals were divided into 30-s epochs for sleep scoring according to the AASM. We extracted middle 10-s segments from these epochs for analysis. Segments with obvious artifacts were removed by visual inspection. In total, 17127 segments of normal controls were obtained (530 W epochs, 2591 R epochs, 515 N1 epochs, 7033 N2 epochs, and 6458 N3 epochs). For signal preprocessing, EEG signals were filtered via a fourth-order zero phase shift Butterworth band-pass filter (0.5-60 Hz).

D. Spectral Analysis

The power spectral density of each segment was determined by Burg autoregressive estimation with 1-s Hamming windows, where the order of the autoregressive model was obtained using the Akaike information criterion [15].

E. Directionality Analysis

PTE was used for information transfer network research in this study. This method is an extended algorithm of TE analysis, which considers the phase data and has the advantages of more robustness to noise and linear mixing and more accurate information extraction [14]. Suppose $\theta_x(t)$ and $\theta_y(t)$ are instantaneous phase of signal X(t) and Y(t), then PTE is defined as:

$$PTE_{X\to Y} = H\left(\theta_y(t), \theta_y(t')\right) + H\left(\theta_y(t'), \theta_x(t')\right) - H\left(\theta_y(t')\right) - H\left(\theta_y(t), \theta_y(t'), \theta_x(t')\right) \quad (1)$$

where $t' = t - \delta$ is the past time point regarding time lag δ. H means the operator of Shannon entropy. For the given discrete variable I, with a probability distribution $p(i)$, the formula of Shannon entropy is as follows [16]:

$$H_I = -\sum p(i)\log\left(p(i)\right) \quad (2)$$

Likewise, for more than one discrete variable, such as I and J with a joint probability distribution $p(i,j)$, the formula of Shannon entropy is as follows:

$$H_{I,J} = -\sum p(i,j)\log\left(p(i,j)\right) \quad (3)$$

The phase is extracted using a combined Morlet wavelet, which is a high-precision frequency division method. Combined Morlet wavelet was construct by superimposing multiple Morlet wavelets (bandwidth was 2 in this work) with a center frequency spacing of 0.05. Number of Morlet wavelets and the central frequency of the first wavelet were 70 and 0.5 for delta (0.5-4 Hz), 80 and 4 for theta (4-8 Hz), 80 and 8 for alpha (8-12 Hz), 400 and 12 for beta (12-32 Hz). More

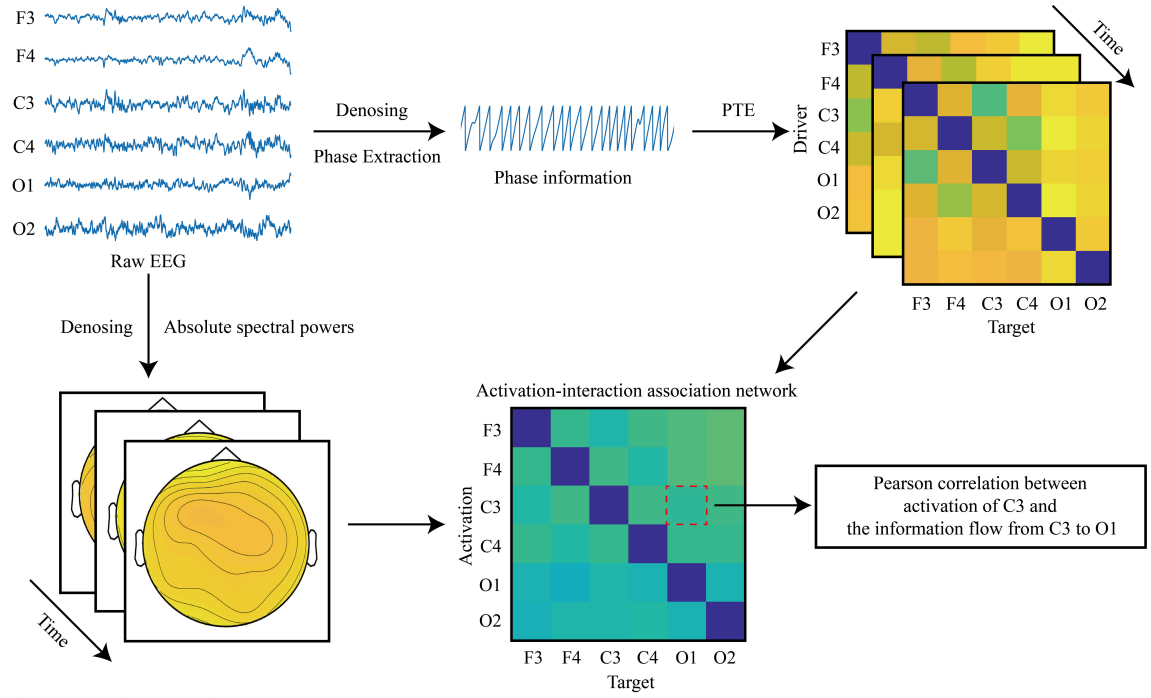

Fig.1 Network construction process

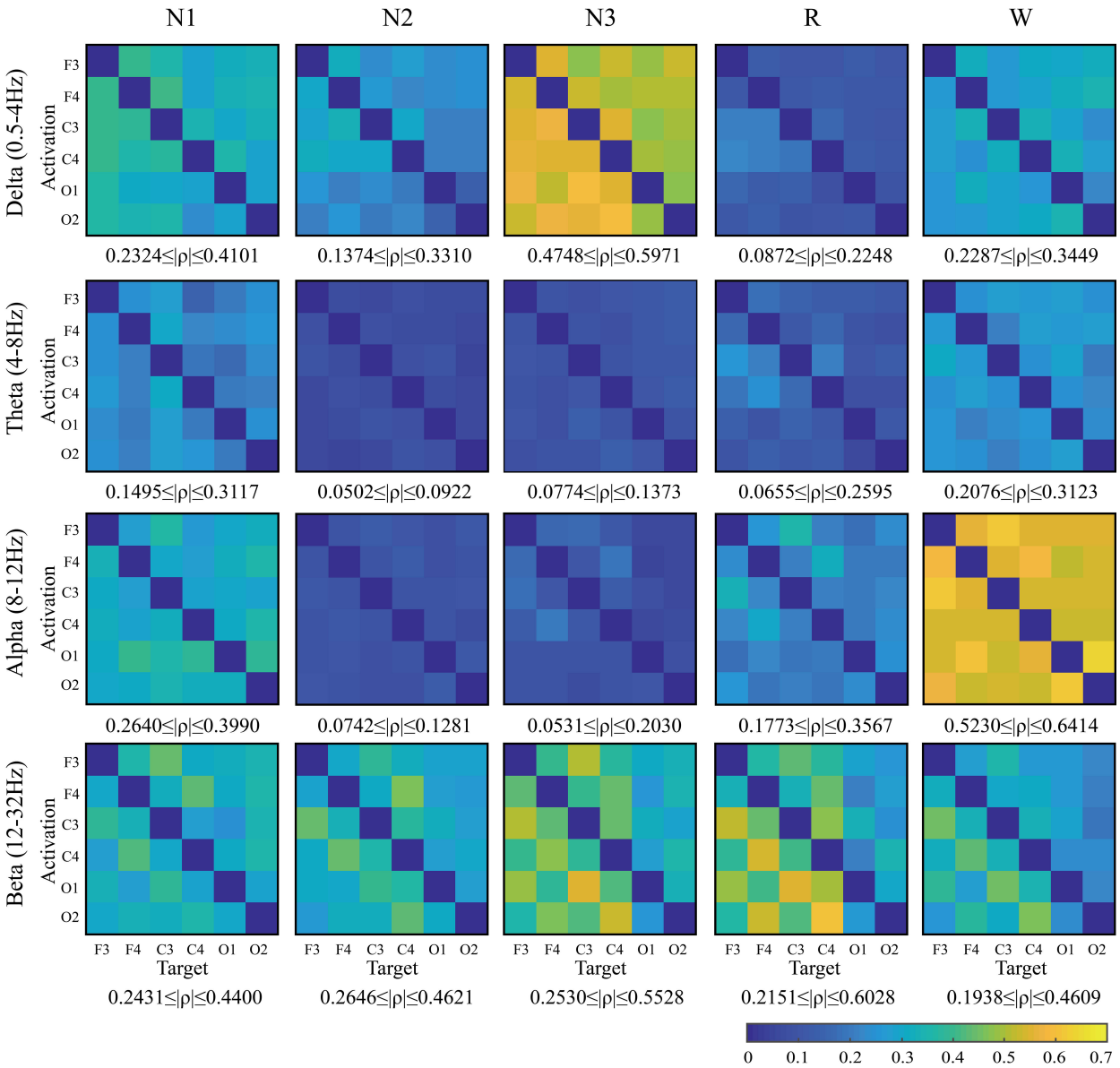

Fig.2 Average activation-interaction associate network in different frequency bands and different sleep stages. The elements of matrix represent the absolute value of the correlation between the activation of the node and information transfer strength from this driver node to a target one. The range of the absolute value of the Pearson correlation coefficient (|ρ|) of each matrix is marked at the bottom of the corresponding matrix.

accurate phase information is extracted via the combined Morlet complex wavelet owing to its advantages of a stable passband, relatively narrow transition band, and good concentration in the time and frequency domains. Thus, we extracted phase of signal in delta, theta, alpha and beta for analysis.

F. Statistical analysis

In order to explore the association between cortical activation and network connectivity during sleep, Pearson correlation test was used to calculate the correlation coefficients between absolute spectral powers and PTE values in different frequency bands and sleep stages. We calculated the absolute value of the correlation ($|\rho|$) between the activation of node A and the flow of information from A (the driver) to other node (the target), and then constructed an activation-interaction association network based on this. The construction process is shown in the Fig.1.

III. Results

The group-averaged results revealed the correlation between the cortical activation and network connectivity during sleep (Fig.2). The association between the absolute spectral powers and the PTE displayed different in researched sleep stages, showing a certain regularity.

In delta frequency band, the correlation matrix showed an increasing performance as the sleep stage deepened, and the color of the matrix was brightest ($0.4748 \leqslant |\rho| \leqslant 0.5971$) during the deep sleep stage (N3).

However, the change of this correlation was relatively not obvious in theta and beta bands with the transition of sleep period. But a certain regularity, attenuated association values with the deepening of the sleep period, displayed in alpha band. The matrix values were highest ($0.5230 \leqslant |\rho| \leqslant 0.6414$) during

the waking period, which was the opposite of the delta band observations.

IV. Discussion

This study investigated association between cortical activation and network connectivity during sleep based on the absolute spectral powers and the PTE derived from cortical EEG. Cortical activation and cortical interactive activities showed an evident association during sleep, and this association changed regularly with the transition of sleep period in special frequency bands. The findings obtained in our research may further indicate the necessity of reporting the results from the spectral analysis concomitant with those obtained from connectivity analysis. Our research may be conducive to the exploration of cortical activity during sleep, allowing us to conduct research from a more comprehensive perspective, avoiding the overestimation and over interpretation of the results brought by a single research method.

The correlation changes significantly in the delta band and the alpha band with the transition of sleep periods. The delta wave is the characteristic wave of deep sleep, and the alpha wave is the dominant wave of our daily activities when we are awake. Electrophysiological experiments showed that sleep onset caused subcortical inactivation and decoupling, which was then reversed in a deeper stage [17],[18]. Additionally, the synaptic homeostasis hypothesis from physiological research put forward the view that enhanced synaptic strength during the day and attenuated strength for normalization during sleep at night [19]. Our results may further indicate that this subcortical inactivation and decoupling of sleep is frequency-specific and may be related to sleep depth. This subcortical decoupling may be mainly reflected in the alpha band, and with the deepening of sleep, the phenomenon of inversion occurs in the delta band. Previous studies found that the adjustment of brain function during sleep involved brain rhythms cross-frequency collaboration [20], which was thought to facilitate information processing during sleep [21]. Moreover, temporal coupling of delta and sigma (10-16 Hz) in non-rapid eye movement sleep was considered to be important for brain recovery and memory consolidation [22]. The frequency band-specific changes (mainly the opposite event in delta and alpha bands) that we found may be related to the cross-frequency coupling mechanism and may contribute to sleep-dependent information integration.

This article mainly revealed the collaboration between cortical activation and cortical information interaction during sleep. To further more comprehensive research on association between observations derived from these two analysis patterns during sleep, the sample size needs to be further expanded and the number of EEG channels will be upgraded to 16 for analysis; cross-frequency research will be further investigated.

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